UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/142,660	12/23/98	HINTSCHE R	60953/119

HM12/1208

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EXAMINER	
SISSON, B	
ART UNIT	**PAPER NUMBER**
1655	8

DATE MAILED: 12/08/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/142,660	Rainer Hintsche et al.
Examiner	**Group Art Unit**
Bradley L. Sisson	1655

☒ Responsive to communication(s) filed on 23 Dec 1998

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 1-20 is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-20 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 7

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Specification

1. The disclosure is objected to because of the following informalities:

a. The subject application has been filed with figures. Figure 1 consists of panels A-E. Each of these panels is considered to be a separate figure. Accordingly, applicant is urged to consider amending the specification so as to reflect Figures 1A-1E.

The specification has been found to contain references to claims. The wording, and the very existence of the claims is subject to amendment. Further, the final numbering of the claims should the subject application be passed to issue, is subject to revision. Accordingly, no reference to claims should be made in the specification.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for coating of an electrode with SH-biotin and detection/measurement of B-galactosidase and p-aminophenol, does not reasonably provide enablement for the detection of any

chemical in any type of sample. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. As presently worded, the claimed method encompasses the detection of virtually any type of compound, or group of compounds, in any type of sample. As required in claim 1, the only independent claim currently pending, the sample is to be applied to an ultra-microelectrode arrangement. The methods disclosed, including those presented in the examples, point to the use of purified solutions of target compounds, not to the use of biological samples for the quantitation of one of a multitude of compounds. Clearly, the use of heterogeneous solutions present a plethora of difficulties; e.g., just which compound is one measuring/detecting, how do you measure the "reverse" of a same, etc. The specification does not set forth a repeatable procedure whereby one would be able to measure any compound, much less any compound present in a heterogeneous solution. It is well settled that the specification, not one of ordinary skill in the art, needs to provide the novel aspects of the invention. See *Genentech Inc. v. Novo Nordisk A/S* 42 USPQ2d 1001 (CAFC 1997). In *Genentech* the court heard argument that the specification of a patent did not contain sufficient detail concerning the practice of a claimed method (*i.e.*, use cleavable fusion expression to make hGH without undue experimentation); *Ibid*, 1004. As set forth at page 1005:

> Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536. 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out

> the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention....
>
> [2] It is true, as Genentech argues, that a specification need not disclose what is well known in the art. *See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate written description.

The claimed method encompasses measurement of binding relationships as well as the unbinding of compounds, e.g., hybridization of nucleic acids to complementary sequences as well as the dissociation of same. The specification is silent as to just how these measurements are to be effected. In view of the limited guidance provided, applicant is urged to consider limiting the breadth of scope of protection sought to those embodiments adequately disclosed and enabled by the subject application.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 1 recites the limitation "the ultra-micro range" in line 7. There is insufficient antecedent basis for this limitation in the claim. Claims 2-20, which depend therefrom, fail to overcome this issue and are similarly rejected.

6. Claim 16 recites the limitation "the active electrode surfaces" in line 2. There is insufficient antecedent basis for this limitation in the claim. Claim 14, which depends therefrom, fails to overcome this issue and is similarly rejected.

7. Claim 18 recites the limitation "the micrometer" in lines 4-5. There is insufficient antecedent basis for this limitation in the claim.

8. Claim 20 recites the limitation "the active electrode surfaces" in line 2. There is insufficient antecedent basis for this limitation in the claim.

9. The term "ultra-microelectrode arrangement" in claim 1 is a relative term which renders the claim indefinite. The term "ultra-microelectrode arrangement" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Claims 2-20, which depend therefrom, fail to overcome this issue and are similarly indefinite and rejected.

10. The term "ultra-micro range" in claim 1 is a relative term which renders the claim indefinite. The term "ultra-micro range" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Claims 2-20, which depend therefrom fail to overcome this issue and are similarly indefinite and rejected.

11. Claims 7, 8, 10-15, and 19 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 has been found to be effectively nonsensical which is due in part to the repeated use of the alternative.

Claim 8 is indefinite with respect to just what are the species bound to. Are they part of the electrode's surface or are they simply on it? Claims 11-14, which depend therefrom, fail to overcome this issue and are similarly indefinite and rejected.

Claim 10 is indefinite with respect to just what the molecules are "fixed" to.

Claim 11 is indefinite with respect to just what constitutes the "reverse." Additionally, the claim fails to recite sufficient method steps that permit the measurement of the forward, or reverse, of any compound, complex, or mixture thereof. What is added to form the complex, or to cause dissociation of same?

Claims 13 and 14 are indefinite with respect to just what constitutes "this event."

12. Claims 13 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: How the support or surface of the electrode is prepared; how the hybridization reaction is performed and/or how the dissociation of complementary strands is effected and analyzed; and how one can differentiate between multitudes of different nucleic acids in a given

sample or between differing degrees of complementarity. As set forth in Carrico, (US Patent 5,200,313) the extent and specificity of hybridization is affected by the following principal conditions:

1. The purity of the nucleic acid preparation.

2. Base compositions of the probe - G-C base pairs will exhibit greater thermal stability than A-T or A-U base pairs. Thus, hybridizations involving higher G-C content will be stable at higher temperatures.

3. Length of homologous base sequences- Any short sequence of bases (e.g., less than 6 bases), has a high degree of probability of being present in many nucleic acids. Thus, little or no specificity can be attained in hybridizations involving such short sequences. From a practical standpoint, a homologous probe sequence will often be between 300 and 1000 nucleotides.

4. Ionic strength- The rate of reannealing increases as the ionic strength of the incubation solution increases. Thermal stability of hybrids also increases.

5. Incubation temperature- Optimal reannealing occurs at a temperature about 25° - 30° C below the melting temperature for a given duplex. Incubation at temperatures significantly below the optimum allows less related base sequences to hybridize.

6. Nucleic acid concentration and incubation time- Normally, to drive the reaction towards hybridization, one of the hybridizable sample nucleic acid or probe nucleic acid will be present in excess, usually 100 fold excess or greater.

7. Denaturing reagents- The presence of hydrogen bond-disrupting agents, such as formaldehyde and urea, increases the stringency of hybridization.

8. Incubation- The longer the incubation time, the more complete will be the hybridization.

9. Volume exclusion agents- The presence of these agents, as exemplified by dextran and dextran sulfate, are thought to increase the effective concentrations of the hybridizing elements thereby increasing the rate of resulting hybridizations.

Further, subjecting the resultant hybridization product to repeated washes or rinses in heated solutions will remove non-hybridized probe. The use of solutions of decreasing ionic strength, and increasing temperature, e.g., 0.1X SSC for 30 minutes at 65 C, will, with increasing effectiveness, remove non-fully complementary hybridization products. The claims currently before the office are, however, silent as to what steps need to be taken in order to achieve any specific desired result.

Claim 19 is confusing as to just how the electrodes are insulated from one another yet can be intersecting with one another. Seemingly these are mutually exclusive events.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. from 5 p.m. to Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-7230.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

B. L Sisson

BRADLEY L. SISSON
PRIMARY EXAMINER
GROUP ~~1800~~ 1650

12-7-99